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Relationship Between Physiological and Clinical Measures of Prospective Memory in Individuals with Mild Acquired Brain Injury, Severe Acquired Brain Injury and Healthy Adults

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RELATIONSHIP BETWEEN PHYSIOLOGICAL AND CLINICAL MEASURES OF PROSPECTIVE MEMORY IN INDIVIDUALS WITH MILD ACQUIRED BRAIN INJURY, SEVERE ACQUIRED BRAIN INJURY AND HEALTHY ADULTS

BY

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Abstract

Prospective memory (PM) involves the ability to form and realize intentions after a time delay (Einstein & McDaniel, 1990). This study examines the relationship between clinical measures of PM and an event-related potential paradigm (West & Ross-Munroe, 2002). Electrophysiological and behavioral data were collected while subjects performed a computerized laboratory PM measure and was compared to a clinical measure, the Memory for Intentions Screening Test (MIST) (Raskin, Buckheit, & Sherrod, 2011) in healthy adults (HA), individuals with severe acquired brain injury (sABI) and mild acquired brain injury (mABI). Individuals with sABI performed significantly worse than individuals with mABI and HA on all variables of the MIST. Individuals with sABI showed reduced amplitude for ERPs that have been associated with intention formation and intention retrieval when compared to individuals with mABI and HA. In addition, total score on the MIST was related to variables associated with attention retrieval. Overall, these findings suggest that individuals with sABI have deficits in PM compared to individuals with mABI and HA and that the MIST may be a valid measure of underlying brain processes of PM.

Introduction

Prospective Memory

Prospective memory (PM) involves the ability to form and realize intentions after a time delay. PM can be described as the memory involved in remembering to do something in the future (Einstein &McDaniel, 1990). As highlighted by Einstein and McDaniel (1990), PM differs from retrospective memory, which is the recall of past events. Since PM depends on the recall of events to be done in the future, it is an indispensible part of independent living. Prospective memory tasks fall into two main categories, time-base and event-based. Time-based PM tasks include remembering to do something at a specific time while event-based PM describe tasks of remembering to perform an action in response to an external cue. An example of time-based PM is remembering to call the florist at noon and example of an event-based PM is remembering to water the plants after seeing a watering can (Einstein and McDaniel 1990).

PM has several distinctive characteristics: formation of a conscious intention; a delay between the encoding of the intention and the intention's execution; a continuous task within the delay; and finally a cue or reminder (Raskin, 2009). These characteristics form the five phases of PM, which are intention formation, a delay period, a performance interval, and realization and monitoring (West & Ross- Monroe, 2002). While these phases are consistent in all PM tasks, research has revealed that HA vary in PM performance. Performance in healthy adults differs between event and time-based cues,

long and short delay periods, action responses and verbal responses (Koriat et al. 1990). In particular, time-based tasks are harder to remember because they require larger amounts of self-initiation and there is no external stimulus to cue and remind the individual of the intended action as in an event-based task (Tay et al., 2010). Another theory of prospective memory suggests that prospective remembering is sometimes aided by strategic monitoring of the environment for appropriate and helpful cues. These cues tend to be a specific event or the passage of a certain amount of time for the completion of an activity (Einstein and Mc Daniel, 2007).

Multiple studies have revealed that the various phases of PM are mediated by prefrontal lobe activity, a finding uncovered through both fMRI (Volle, Gonen-Yaacovi and Burgess, 2011) and EEG (West & Ross-Munroe, 2002, West, 2011). This finding is further supported by complimentary EEG studies, which reveal that the parietal and occipital regions of the brain are also involved in the monitoring processes that underlie successful prospective memory performance (Chen et al., 2007; Chen et al., 2009; Cona et al., 2012; West et al., 2007). The brain regions identified by these imaging studies provide a preliminary map, enabling further investigation into the processes of PM.

Laboratory measures of PM used in these studies tend to be very simplistic. The experimental protocols of these PM studies, which examine correlates, tend to consist of regimented computer-based tasks. These tasks, by nature of their fMRI and EEG experimental design, tend to lack the naturalistic aspect of prospective memory. Thus, it is interesting to compare imaging measures with a more clinical measure of PM. My study aims to combine investigation of neural correlates with the measurement of clinical elements of prospective memory to provide a better view and understanding of this

cognitive process.

Mild Acquired Brain Injury and Severe Acquired Brian Injury

Criteria for mABI and sABI

PM impairment has been found to follow brain injuries both mild (Tay et al. 2010) and severe (Shum, Levin and Chan, 2011). Problems in PM are a common symptom post brain injury (Raskin 2009). Unfortunately, the neurological correlates of these PM errors are elusive. Therefore examining PM in these populations with both ERP and behavioral analysis provides insight into PM function.

Acquired brain injury (ABI) is defined as a brain injury that has occurred after birth (Brain Injury Association of America, 2012). ABI provides a broad umbrella definition, and, depending on the severity of the injury, can include etiologies such as cerebrovascular accidents (CVAs) or strokes, and encephalitis (Brain Injury Association of America, 2012). ABI does not include brain injury that is congentital, hereditary, degenerative or induced by birth trauma. ABI includes Traumatic brain injury (TBI), a type of ABI that refers to structural injury that has been induced traumatically and or a physiological disruption of brain function resulting from an external force (Vincent, Roebuck-Spencer & Cernich, 2014). In a TBI the injury is a result of a blow that causes opposing movement between the brain and the skull. This blow generates centripetal, percussive and shearing forces that result in TBI (Duff, 2004).

An ABI is specifically indicated by new onset or worsening of at least one of the following clinical signs immediately following the event: any time interval of loss of consciousness, any loss of memory for occurrences immediately before or after the accident, any change in mental state at the time of the accident (such as being perplexed, bewildered and disoriented), and principal neurological deficits such as change in vision, sensory loss, aphasia, loss of balance and weakness. These neurological deficits may be experienced briefly or persist for weeks, months or even years (American Congress of Rehabilitation Medicine, 2012).

The most common assessment measure of ABI severity is determining the depth of coma. This is done using the Glasgow Coma Score (GCS) and establishing the duration of unconsciousness after injury. A few methods of determining this are determining the loss of consciousness, assessing the time to follow commands, and the duration of confusion after injury, for example, the length of posttraumatic amnesia (PTA) (Vincent et al., 2014). The severity of an ABI ranges from mild to moderate to severe with disruptions in cognitive, behavioral, emotional, or physical function. Depending on the characteristics and severity of the injury these effects may be short-lived, long lasting, or permanent depending on injury characteristics and severity (Carroll et al., 2004).

For an ABI to be considered mild (mABI), thirty minutes after injury, there must a Glasgow Coma scale (GCS) of no less than 13. If there is a loss of consciousness it must be brief; thirty minutes or less and, if present, any posttraumatic amnesia must not exceed 24 hr. These criteria include brain injuries such as the head striking an object, an

object striking an object and the brain then undergoing whiplash: deceleration or acceleration. This definition includes brain injuries that have been diagnosed or described as concussions. mABI does not include tumors, stroke anoxia, and encephalitis. Importantly, several forms of neuroimaging such as magnetic resonance imaging, electroencephalogram and other routine neurological evaluations may be normal after suffering a mABI.

On the farther extreme, when there is a GCS of (8-13) post-injury, a loss of consciousness of greater than 30 minutes, or PTA greater than 24 hr, then the brain injury can be classified as a sABI (American Congress of Rehabilitation Medicine, 2012).

Symptoms of mABI

Symptoms of mABI can be divided into three main categories: physical changes, cognitive deficits and behavioral changes. Firstly, physical symptoms include dizziness, headache, vomiting, blurred vision; sleep disturbance, lethargy, and quickness to fatigue that do not result from other injuries or causes (American Congress of Rehabilitation Medicine, 2012). Secondly, cognitive deficit symptoms include symptoms not caused by other emotional states and disorders that implicate attention, perception, concentration, memory, speech production or executive functions. Lastly, symptoms that involve behavioral and emotional changes not attributed to other forms of physical and emotional stress and psychological response. Such behavioral symptoms may include emotional disinhibition, irritability, emotional volatility and quickness to anger (National Institute of Neurological Disorders and Stroke, 2014). The aforementioned symptoms and criteria of

mABI can also be described by numerous terms such as post-brain injury symptoms and posttraumatic syndrome, in the case of an ABI involving trauma, minor head injury, traumatic cephalgia, traumatic head syndrome, and post-concussive syndrome (American Congress of Rehabilitation Medicine, 2012). In mABI, these post concussion syndrome symptoms usually dissipate quickly, but some individuals report persistent symptoms that span weeks, months and even years post injury. Although there are multiple categories of symptoms and multiple symptoms within each category, many of these symptoms can be missed when emphasis is given to more tangible physical and sometimes more dramatic injuries post accident. Unfortunately the cost of this oversight can mean that individuals do not receive the medical care and advice needed to limit long term effects of mABI.

Symptoms of severe acquired brain injuries (sABI)

Symptoms of sABI (GCS 8-13) (Brain Injury Association of America, 2014) include confusion that lasts for upwards of a week, and physical, cognitive and behavioral impairments that span months or become permanent. sABI with a GCS below 8 follows when an individual has experienced an extended state of unconsciousness spanning days, weeks or months. According to the Brain Injury Association of America (2014) sABI (GCS below 8) is then further classified by the following subgroups that each carries distinctive features. There are five main groups including coma, vegetative state, persistent vegetative state, minimally responsive state, akinetic mutism and locked-in syndrome.

Prognosis of mABI

Mild acquired brain injury includes brain injuries that have been sustained after birth and comply by the criteria of ABI. The prognosis of mABI and sABI has substantial differences. In cases of a mABI, symptoms are rectified quickly and there is insignificant proof of long lasting deficits (Carroll, Cassidy, Peloso, Borg et al. 2004). During the acute stage following a mABI, adults commonly experience cognitive deficits and symptoms. Despite the prevalence of initial symptoms, based on studies involving mABI adults, most adults with mABI recover within 3-12 months (Carroll et al., 2004). Prior health status, age and life stress is also important for the prognosis of mABI (Carroll et al. (2004)

Prognosis of sABI

The prognosis for adults with sABI is more varied and depends on factors such as age, GCS score, pupillary response and size, high intracranial pressure, hypoxia and hypothermia (Jiang et al., 2002). Based on a study of 846 severe TBI cases, at one year post injury, the outcomes were 31.56% good recovery, 14.07% moderate disability, 24.35% severe disability, 0.58% vegetative status, and death 29.43% (Jiang et al. 2002). Like Carroll et al. (2004) Jiang et al. (2002) state that other factors can provide indicators of prognosis for individuals with severe head injury and that efforts to reduce the negative effects of these factors can improve the overall prognosis. In particular, the control of high intracranial pressure, the prevention of hypoxia and the prevention of hypothermia have the potential to ameliorate the outcome of individuals with sABI.

Since individuals with ABI often have PM deficits, examining PM in these populations has the potential to provide valuable insight into PM function. Since PM has become a topic of investigation, several clinical tools have become available to measure this cognitive process. Both clinical and electrophysiological testing tools presently enable investigation of PM.

PM in individuals with ABI

mABI

mABI is consistently linked to damage in three brain areas, the frontal lobe, the temporal lobe and the parietal lobe (Duff, 2004). These areas are central to cognitive processes involved in successful PM performance. The effect of cumulative concussions (mABIs) has been found to attenuate an ERP, P3 that is linked to bottom up visio-spatial attentional processing (Thériault, Beaumont, Tremblay et al. 2010). In this study, athletes with a history of 3 or more concussions (mABIs) showed significantly reduced sustained posterior contralateral negativity (SPCN) relative to both concussed athletes with one or two prior concussions and athletes with no concussions (mABIs) (Thériault et al., 2010). While the SPCN waveform, which provides a visual memory capacity estimate did not differ significantly between groups, the study's findings suggest that altered working memory (WM) may worsen with aging and additional brain insults since concussive injuries were found to induce changes in the ability to activate or modulate working memory (WM) processing resources (Thériault et al., 2012). While visio-spatial attentional processing and working memory has not been explicitly linked to PM, the

effect of mABIs on these two ERPs begs investigation into the effect of mABI on another cognitive process, PM. Additionally, a study by Carlesimo, di Paola, Fadda et al. (2014) underscored the role of the frontal lobe (BA 10) in fundamental aspects of attention, which are critical in performing previously formulated attentional tasks. Such tasks are indispensible to performing PM successfully. Therefore, it follows that individuals with mABI may encounter problems with PM performance, since studies have shown that damage or alternation to the prefrontal lobe is the most frequent finding in individuals with ABI (Shum, 2010;Volle, Gonen-Yaacovi and Burgess, 2011; West & Ross-Munroe, 2002, West et al. 2007; 2011).

While PM challenges in some individuals with mABI persist, most individuals with mABI recover from cognitive deficits and Post Concussion Syndrome (PCS) symptoms in the weeks after the injury (Carroll et al., 2004). At the same time, there is also a consistent group of individuals with mABI who have persistent cognitive deficits and Post Concussion Syndrome (PCS) symptoms. Therefore, it can be expected that the majority of individuals with mABI experience little to no PM deficits, but there may be a percentage of the mABI population with persistent symptoms who may experience PM challenges with successful PM execution.

sABI

Individuals with sABI have significantly reduced successful performance in PM tests compared to HA with no ABI, on both event and time based PM (Shum et al., 2010). Additionally, in another study, participants with sABI (specifically sTBI)

experienced great difficulty allocating attentional resources to the PM task, as well as discriminating PM targets from non-targets during PM trials (Pavawalla, Schmitter-Edgecombe & Smith, 2012). Individuals with sABI are impaired on time, event and activity based PM compared to controls (Vakil, 2005). The consistent findings among these studies provide a clear picture of PM deficit in individuals with sABI.

PM assessment tools

Memory for Intentions Screening Test (MIST) and Cambridge Test of Prospective Memory (CAM-PROMPT)

Investigating PM requires systematic measurement of the established stages of PM by testing elements of both time and event based tasks. The Memory for Intentions Screening Test (MIST) (Raskin and Buckheit, 1998) is a behavioral test that evaluates this function. It is a standardized clinical measure of PM that measures the multiple cognitive processes that are involved in the performance of PM (Raskin 2009). Another standardized test is the Cambridge Test of Prospective Memory (CAM-PROMPT). Which measures three time-based tasks, three event based tasks and an ongoing task. A unique identifying element of CAM-PROMPT is that subjects are allowed to take notes throughout the test and plan their actions to the tasks (Fleming, 2008).

While both the MIST and CAM-PROMPT have both event and time based tasks, the MIST differs in the following ways. The MIST lasts 30 min and demonstrates clinical specificity and sensitivity (Raskin 2009). In addition, the MIST is appropriate for a wide

age group adults aged 18-95 years old. Within the MIST, the ongoing task is a word search. More specifically, the MIST assesses the two types of PM cues (event-and-time-based cues), different types of responses (verbal or action), different delay periods (2-15 min), and specific PM errors. These errors include: 1) PM failure (PF) in which the subject does not give a response; 2) Task substitution (TS) in which the participant performs an action for a verbal item or a verbal response for an action item; 3) Loss of content (LC) when the subject remembers that a task needs to be done at the correct time but cannot remember what the task was; 4) Loss of time (LT) in which a task was recalled correctly but at the wrong time; 5) the place losing error (PL) in which the participant did only part of the task or repeated a previous task; and lastly, random errors (RE) when the subject's error does not match any error categories (Raskin 2009). Taking these errors and the other variables into account, the MIST provides a thorough analysis of multiple areas of failures therefore allowing an in depth testing mechanism for the behavioral elements of PM.

The design of the MIST also allows for assessment of PM in different populations and thus forms an effective tool for comparison of PM function across clinical populations. Studies using MIST involving healthy adults and individuals with mTBI have revealed interesting similarities and differences between the populations. MIST studies have shown that individuals with mTBI had significant impairment on event cues and the 24-hr trial (Raskin, 2004). Both the control and mTBI groups performed better on action responses over verbal responses. In addition, the only error type was PM errors. Raskin (2004) interpreted these findings to mean that individuals with mTBI may have difficulty performing tasks that require complex attention. This attention is indispensible

to observing the time and keeping the intention in mind: abilities that facilitate PM. These findings encourage further research into the PM performance of populations with known PM deficits such as individuals with varying degrees of ABI.

Electrophysiological correlates of PM

Electrophysiological correlates provide another method of measuring and analyzing PM. Event-related potentials (ERPs) are a useful for investigating the brain regions and activity related to PM. ERPs can be defined as electrical brain responses resulting from an external stimulus such as an image on a computer screen. ERPs are reflected by a positive or negative voltage deflection over a course of time (West, 2011) ERPs are measured from the scalp using an electroencephalogram (EEG) machine and are locked to a specific time in response to a specific event. ERPs are described by their polarity and are denoted by P for positive and N for negative (West, 2011). West's ERP paradigm (West 2001, West and Ross-Munroe, 2002) uses ERPs to examine the five phases of PM using an EEG machine and the partial cue PM task. This task only assesses event-based PM and includes two different trials: ongoing activity and PM cue (West, 2003). West's most recent and comprehensive experimental design (West & Ross-Munroe, 2002) includes a computer-based test where the individual engages in an ongoing activity and decides if a pair of randomly colored words are semantically related or unrelated and responds by pressing one of two keys on a keyboard labeled 'same', for related words, or 'different', for unrelated words. This ongoing activity fulfills the PM requirement for a continuous task within the delay. The measurement of related and

unrelated word accuracy and reaction time provides a measure of ongoing activity engagement. Measuring these related and unrelated elements of the ongoing activity provides insight into the performance and level of active involvement for the ongoing task. Then, as the ongoing activity proceeds, the intention formation trial, also referred to as the PM cue, is presented (a string of letters: c or v in either grey or magenta). Then, several word pairs later (in colors other than grey or magenta) a word pair in either grey or magenta is shown. At this point the subject has to remember the color and letter (c or v in grey or magenta) seen previously in the PM cue string, and press the corresponding letter that was most recently associated with the presented word pair color (West 2001). If the participant makes a correct PM response and presses the letter (c or v) that corresponds to the presented grey or magenta colored word pair, they have successfully realized the intention. This is considered a PM hit or a correct PM response. If the participant fails to press the corresponding letter when presented with a pair of words in grey or magenta, they have not realized the intention. Therefore, this is an unrealized intention, and can also be described as an incorrect PM response, or a PM miss. During this task an EEG machine monitors brain activity and records ERPs. Behavioral and electrophysiological variables from the ongoing activity can then be compared to PM cue variables since these elements of the test measure performance on the separate elements of PM, for example, involvement in the ongoing activity, disengagement from the ongoing task, and PM performance. West (West 2001, West & Ross-Munroe, 2002) showed that the ERPs produced on the ongoing activity and PM cue trials were each different and thus distinguishable (Figure 1, 2).

These differences facilitate the identification of the different physiology for the detection of a PM cue, recovery of an intention from memory and its realization (West, 2003). In an earlier study (West, 2001) the PM cue was ambiguous because it did not allow differentiation of neural activity associated with the formation and realization of an intention. The ability to differentiate these phases of PM is central to understanding the neural correlates, thus adjustments were made to the PM cue. These changes were then added to the stimulus of West & Ross-Munroe (2002).

The modified PM cue stimulus identified specific PM ERPs. The distinct ERPs associated with PM are N300, parietal positivity, LPC (late positive component), and slow waves (West 2003). The N300 and parietal positivity are the neural correlates associated with the realization or detection of intentions on PM. The N300 is a phasic negativity that occurs 300ms after stimulus onset, peaking over the occipital parietal region (West & Ross-Munroe, 2002) (Figure 3,4), while the parietal positivity is an extended positivity over the parietal region of the scalp between 400 and 1200ms after stimulus onset, (West, 2011). The N300 specifically is associated to alerting the neural system to the presence of a possible cue. Late Positive Component (LPC) is the ERP associated with the recovery of an intention from memory. The Late Positive Component (LPC) is reflected positively over the parietal region of the scalp, and negatively over the lateral frontal regions of the scalp 575 ms after stimulus onset (West & Ross-Munroe, 2002)(Figure 5,6). Finally, the slow wave is associated with disengagement from the ongoing activity and alerts to a possible cue (West & Ross-Munroe, 2002;West 2003) (Figure 7,8). The slow wave occurs as a sustained negativity over the frontal-central

region of the scalp, 400ms after stimulus onset (West & Ross Munroe, 2002) (Figure 1,2,3,4,5,6,7 and 8 reproduced from West & Ross-Munroe, 2002).

ERPs for Various Trials

Ongoing Activity

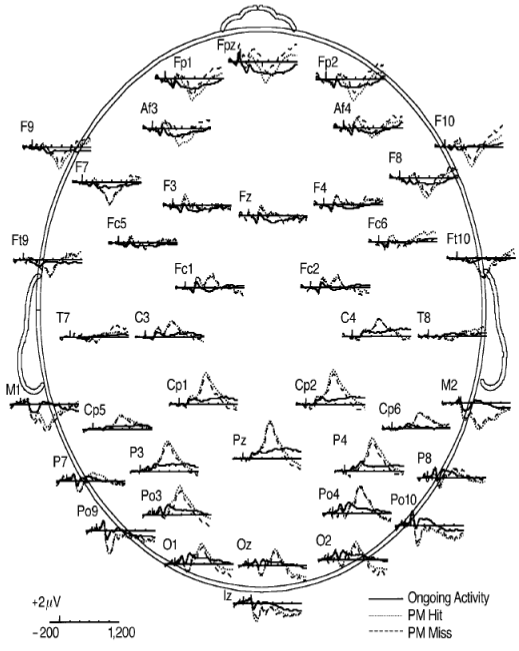

Figure 1. Grand averaged ERPs for ongoing activity trials preceding intention formation trails, realized intention trials, and unrealized intention trials and their approximate spatial locations on the scalp (West & Ross-Munroe, 2002).

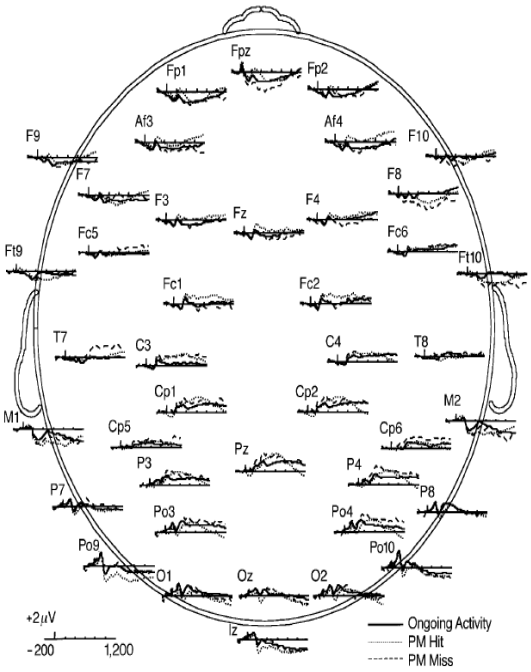

Figure 2. Grand averaged ERPs for ongoing activity trials preceding PM cue trials, PM hit trials, and PM miss trials and their approximate spatial locations on the scalp (West & Ross-Munroe, 2002)

N300

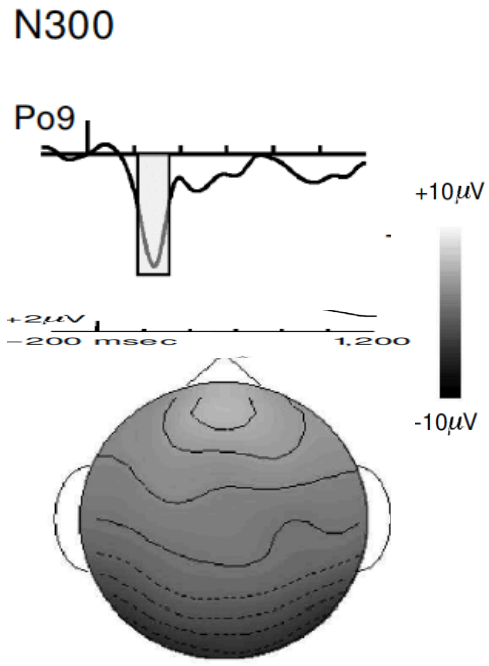

Figure 3. ERP difference waves and spline voltage maps reflecting the N300 for the intention formation trials. The waveform reflects the difference between realized intentional trials and unrealized intention trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).

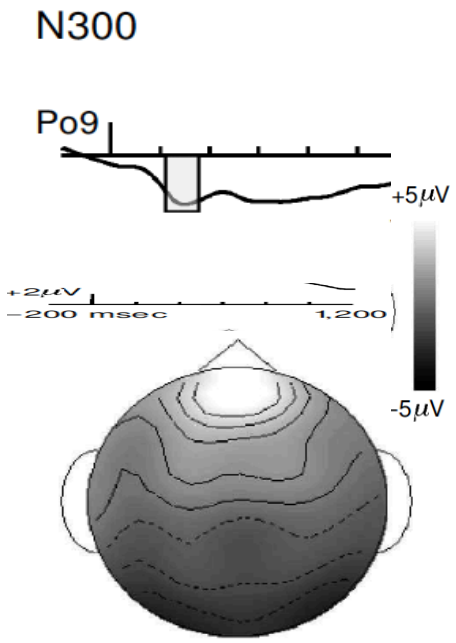

Figure 4. ERP difference waves and spline voltage maps reflecting N300 for PM cue trials. The waveform reflects the difference between the PM hit trials and ongoing activity trials. The topography reflects the activity of the bounded area for each modulation (West & Ross-Munroe, 2002).

Late Positive Component (LPC)

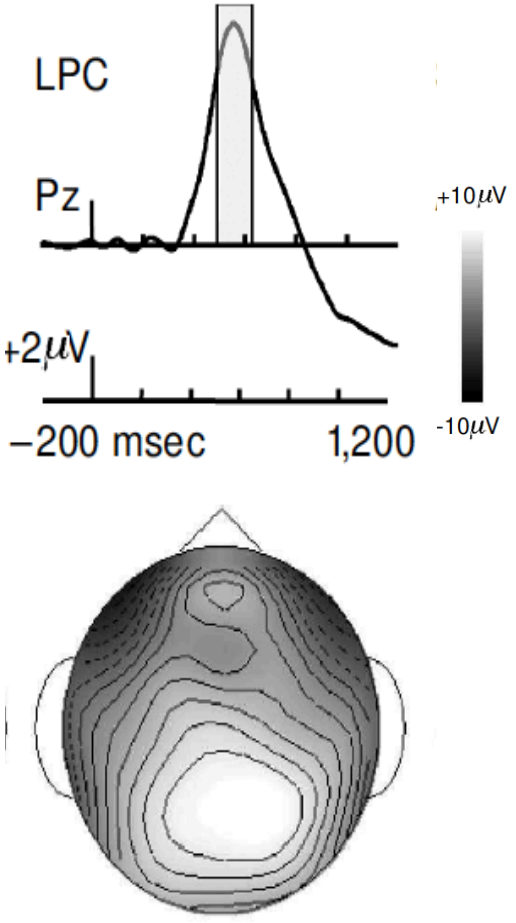

Figure 5. ERP difference waves and spline voltage maps reflecting LPC for intention formation trials. The waveform reflects the difference between the realized intention trials and ongoing activity trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002)

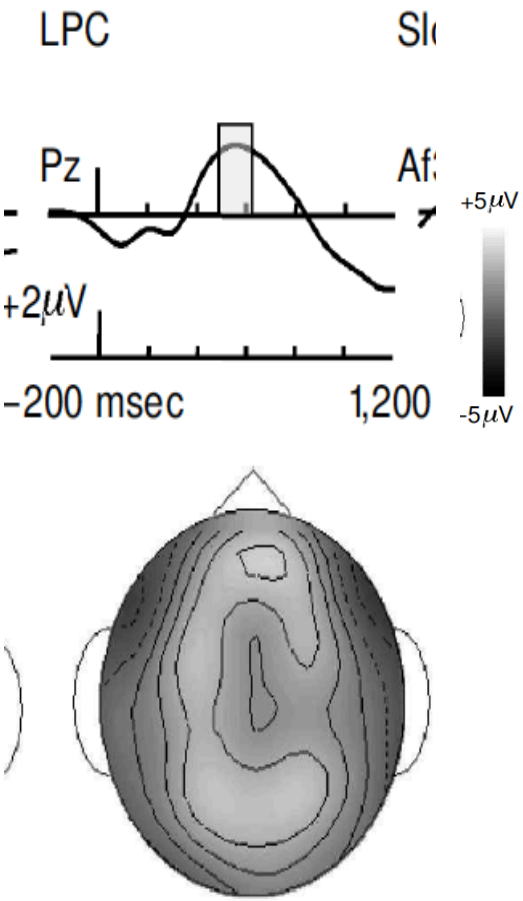

Figure 6. ERP difference waves and spline voltage maps reflecting LPC for PM cue trials. The waveform reflects the difference between PM hit trials and ongoing activity trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002)

SW (Slow Wave)

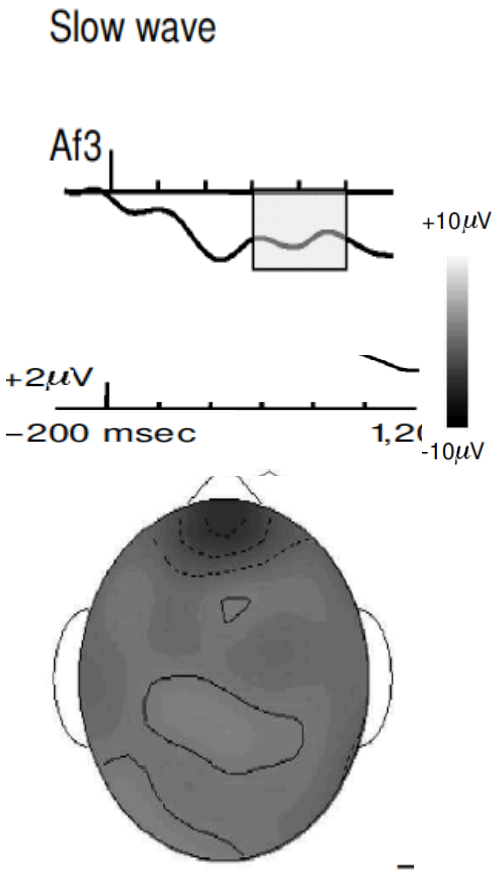

Figure 7. ERP difference waves and spline voltage maps reflecting slow wave for intention formation trials. The waveform reflects the difference between the realized intention trials and unrealized intention trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).

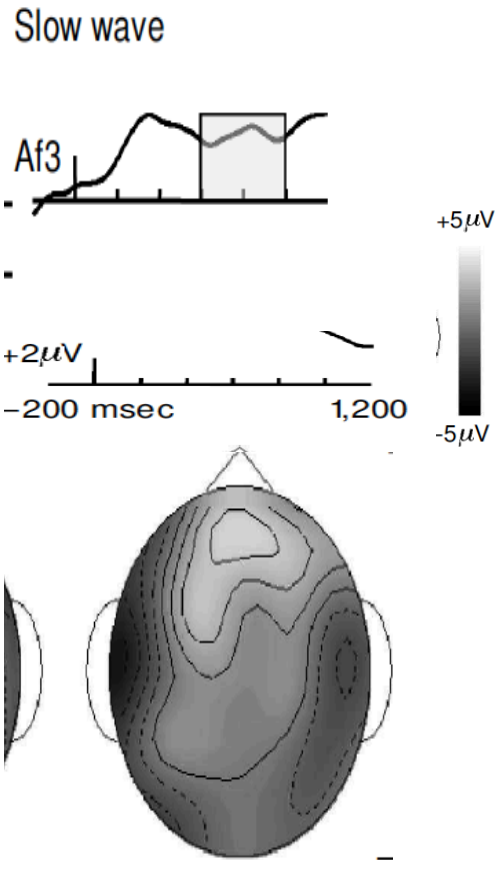

Figure 8. ERP difference waves and spline voltage maps reflecting slow wave for PM cue trials. The waveform reflects the difference between PM hit trials and PM miss trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).

PM Neural Correlates using fMRI

As previously mentioned, neural correlates of PM have been mapped using two forms of neuroimaging: fMRI and EEG. In fMRI studies, the most common finding is that PM is linked to activation in the rostral prefrontal cortex (PFC) (approximating Brodmann Area 10) (Burgess, Gonen-Yaacovi & Volle, 2011). The findings of multiple studies consistently support this finding, specifically in event-based PM paradigms (Burgess et al. 2003). This region is part of a rostral PFC attentional gateway that forms part of the "gateway hypothesis" of rostral PFC function. The gateway hypothesis proposes that a central purpose of rostral PFC is to control differences in attending between "stimulus-independent thought" (i.e. our inner mental thoughts) and thought involved in attending preferentially to the external world ("stimulus-oriented attending") (Burgess, Dumontheil, et al., 2007; Burgess, Gilbert, et al., 2007; Burgess et al., 2006; Burgess, Simons, et al., 2005). This finding and proposed function of the rostral PFC agrees with the mechanisms and stages of prospective memory since successful encoding, intention maintenance, intention retrieval and intention execution all require control of differences in attending.

In PM fMRI studies, there is second brain region that emerges as involved in PM, which is remarkably consistent during PM tasks. Numerous studies have found frequent activation of BA 7 & 40 (precuneus, parietal lobe) as well as the anterior cingulate (BA 32) during PM tasks performance (Burgess et al., 2001). Additionally, some of these regions are frequently co-activated with rostral PFC during many types of cognitive task,

not just PM ones (Burgess et al., 2001). This finding is especially salient since activation in the parietal lobe is also a consistent finding in ERP studies using electrophysiological imaging techniques (West, Herndon, & Crewdson, 2001; McDaniel & Einstein, 2007). fMRI studies have not identified a clear cognitive significance of the activation of the precuneus and parietal lobes (BA 7 & 40), but, according to Burgess et al. (2011), each region likely supports a different aspect of prospective memory. This is illustrated by Hashimoto et al. (2010), who show higher activation in the inferior parietal lobule (BA 40) in control conditions compared to conditions relating to the PM intentions. In the same study, activation of a slightly more superior region BA 40 (inferior parietal lobule 55−56 38) was found during PM blocks.

A recent fMRI and EEG study discovered findings that provide a connection between the different brain regions associated with PM. In this study, two neural routes to PM were found (McDaniel, LaMontagne, Beck, Scullin and Braver, 2013). The first route was in attentional-control areas, such as the anterior PFC and involved sustained activity. The second route recruited only transient activity in parietal and ventral brain regions that are linked with attentional capture, target detection, and episodic retrieval, otherwise known as bottom up shifts of attention (Cabeza et al., 2008). These two connections have adaptive value since multiple routes to PM retrieval is advantageous for achieving successful PM performance in different kinds of situations.

PM neural correlates using ERP analysis

Effect of Age on PM

Recent prospective memory research using ERPs continues to investigate PM in populations of healthy adults. While West examined ERP data in response to PM stimuli (West & Ross-Munroe 2002), other studies investigated the ERP modulations of the ongoing task of PM. In one study examining age differences of PM ERPs, older adults ages 60-67 years lacked prefrontal sustained ERPs that were prevalent in younger adults (21-28 years old)(Cona et al., 2012). This particular ERP modulation, sustained positive activity, was associated with the retrieval mode of PM. Since this modulation was not shown in the older adult cohort, Cona et al. (2012) interpreted this finding to mean that older adults show an impairment of a strategic monitoring system. Cona et al. (2012) further suggest that while this finding was shown during ongoing tasks, this impairment may exist in both time-based and event-based tasks.

Studies examining age differences of PM have also investigated the development of neural correlates associated with the distinct phases of PM. Mattli, Zollig, and West (2011) examined ERPs in response to PM cues. The four ERPs examined were: frontal positivity, parietal positivity, N300 and the slow wave. These ERPs are associated with task configuration (frontal and parietal positivity) cue detection (N300), and disengagement from the ongoing activity (slow wave). All examined ERPs were consistent and reliable across age groups ranging from 7.5 to 83 years old. Mattli et al.

(2011) concluded that these findings indicated that different age groups had the ability to pay attention to and perform PM tasks. Since the youngest participants were age 7.5 years, the authors further concluded that the cognitive resources necessary to perform PM successfully were functional by middle childhood (Mattli et al., 2011). Interestingly, Mattli et al. (2011) found evidence of differences in the processes behind PM errors between children and adults. They suggest that PM errors in children originate from a disconnect between processes that facilitate cue detection and task switching from the ongoing activity to the PM task. By contrast, PM errors made by both younger and older adults seem to result from errors in detecting PM cues in the environment during the ongoing task. The PM cue ERP findings across the lifespan led Mattli et al. (2011) to conclude that PM diversity across different ages is the result of multiple processes. They conclude that different processes that may or may not be unique to each age yield variations in PM function from childhood to late adulthood.

Memory Training Interventions on PM

Other studies have extended the investigation of age effects on PM and neural correlates to include cognitive interventions. In one study, an intervention was designed to improve elements of PM (Zollig, Mattli, Sutter, Aurelio and Martin, 2012) by rehearsing the sequence of the ongoing task event. Sequence rehearsal consisted of memorizing the colors and consecutive positions of colored squares within a 6X5 matrix Participants had to learn both position and color of squares within the matrix. An important element of the intervention sequence training was that participants received the

instructions for both the ongoing and PM task just before the start and not before or during the sequence learning session. Participants rehearsed the sequence but were not aware of the PM cues or their importance while being trained. The control group was made to perform parts of the Wechsler-Memory Scale (WMS-R, Hartling et al., 2000) in order to make cognitive exposure similar to the intervention group.

Zollig, et al. (2012) compared the PM ERPs of a control group and an intervention group. Both the control and intervention group consisted of adults aged 69-93 years old who had reduced PM performance. The control group showed higher activation than the intervention group in the left inferior frontal regions in correct PM trials (Zollig et al. 2012). According to West and Covell (2001) and West, Herndon et al. (2003), in experiments without ongoing task training, there was a reduction in N300 amplitude in older adults and elevated N300 amplitude in younger adults. These studies without ongoing task -training found that the reduced N300 ERP was linked to a decline in the execution of a neural system that supports cue detection. Compared to the control group, the intervention group had an N300 with elevated amplitude in PM trials. This N300 amplitude was similar to the waveform present in young adults with few PM errors. Thus Zollig et al. (2012) concluded that the intervention that familiarized the older adults with the sequence of events increases PM performance. They suggest that the increased familiarity may support better efficiency in monitoring for PM cues. These findings of Zollig et al. (2012) offer hope for the success of clinical interventions and remediation programs as a method of improving the PM function of populations with PM deficits. This study aims to understand the neural correlates of ABI populations that experience PM deficits. The work of Zollig et al. (2012) establishes that such interventions may

reduce the deficits of affected individuals. These promising findings make understanding the neural correlates of ABI populations more urgent as potential solutions seem on the brink of discovery.

Target checking involves scanning the environment for the cue to perform the intention when the cue appears. Scolaro (2012) investigated the neural correlates of target checking as an element of the PM retrieval mode model. Using physiological data, two specific ERPs were linked to target checking: posterior negativity (300-400ms) and LPC (600ms- 1000ms). Results revealed that target checking seems to include an early and late process. The early process appears to involve the representation of a stimulus and the late process seems to involve the retrieval of representations from memory (Scolaro, 2012). These findings provide another valuable perspective from which PM neural correlates can be examined. Two already established PM ERPs linked to target checking can provide insight into the PM deficits of those with mABI and sABI.

This study

This study analyses ERPs to pinpoint differences between healthy adults and those with mABI and sABI. Using an established clinical PM measure (MIST) and a well-validated PM electrophysiological measure (West & Ross-Munroe 2002), I aim to identify the behavioral and neural correlates of PM deficits in these populations and determine any differences between the groups.

Questions and hypotheses

Question 1

What are the specific electrophysiological correlates associated with prospective memory (PM) in healthy adults and individuals with mABI and sABI?

Question 1 Hypotheses

1. Brain injury affects the functioning of neural systems that are involved in PM
2. Deficits in the neural systems associated with PM will be relative to the extent of the brain injury

Question 1 Prediction

3. Healthy adults will have higher performance on clinical and behavioral measure of PM compared to individuals with mABI and sABI.
4. Healthy adults will have higher amplitude on ERPs associated with PM compared to individuals with mABI and sABI

Question 2

How do the electrophysiological correlates of PM relate and compare to the behavioral measures of PM?

Question 2 Hypothesis

1. Loss of PM has a neural basis therefore neural activity can be associated with behavioral correlates of PM.

Question 2 Predictions

1. The PM intention trials with increased activation in frontal lobes will correlate with MIST total score.

2. Those with mABI will show reduced neural activation that is significantly related to the reduced performance on the MIST

Methods

This present study was conducted at Trinity College, Hartford, Connecticut, and was approved by Trinity College's Institutional Review Board (I.R.B). This study investigated and analyzed the relationship between the clinical and physiological measures of PM using a two-step procedure. The complete study took 2 hr. to complete. The first step was a clinical measure, the MIST. The second step, involved the electrophysiological measure, following the West & Munroe (2002) experimental design.

Participants

Demographic information for all three groups of participants is in Table 1. Thirty-six healthy participants formed the control group for this experiment (M= 41.54, SD= 17.44 years, 11 male, 25 female). All participants were right handed. The first experimental group was comprised of fifteen participants with mABI (M= 20, SD= 2.37 years, 7 males and 8 females). Previously collected data from thirty individuals (M= 45, SD= 16.39 year, 17 males, 13 females) with sABI, was also used and analyzed with this experiment, and formed the second group. These participants were recruited from a Brain Injury Association of Connecticut support group, which is hosted at Trinity College and facilitated by Sarah Raskin, Ph.D. Both healthy and participants with mABI were recruited from the Trinity College staff and student body.

The inclusion criteria for healthy adults (HA) consisted of more than 12 years of education, adequate visual and auditory functioning, the absence of neurological or psychological illness and English as their first language.

In recruiting for HA, subjects were excluded if they had ever had a diagnosis of a neurological disorder (e.g Multiple Sclerosis, Parkinson's Disease, Epilepsy, Alzheimer's), significant difficulty functioning independently, a diagnosis of HIV/AIDS, loss of oxygen to the brain (anoxia), a severe head injury, severe visual and hearing impairment that interferes with participation in daily activities, treatment for substance abuse or dependence, or hospitalization for a psychiatric condition.

For individuals with mABI, inclusion criteria consisted of: an acquired brain injury, English as the first language, no other neurological of psychiatric illness, 12 or more years of education, adequate visual and auditory functioning, and at least six months post brain injury. The inclusion criteria for individuals with sABI consisted of: a traumatic brain injury, English as the first language, no other neurological or psychiatric condition, 12 years or more of education, adequate visual and auditory functioning and at least one year post-injury. All participants provided written informed consent prior to testing. Participants received financial compensation of a $15 gift certificate to a campus bookstore or restaurant. Detailed information about demographics, concussion and postconcussion symptoms are summarized in Table 1.

Table 1. Demographic and clinical information

Variable	Healthy	sABI	mABI
N	36	30	15
Age (years)***	41.54 ± 17.44	45 ± 16.39	20 ± 2.37
Male	11	17	7
Female	25	13	8
Years Education**	17.27 ± 3.68	14 ± 2.98	15.17 ± 1.27
Etiology	---------	21 MVA, 5 falls, 1 neurological disorder, 2 CVA, 1 encephalitis	15 concussions

*p<0.05, **p<.01, ***p<.001. *. One-way ANOVA post hoc test significance at the 0.05 level. **.One-way ANOVA post hoc test significance at the 0.01 level.

One-way ANOVA revealed a significant difference in age, $F(2,78)=13.27$; $p<0.001$, between HA and the group with mABI and between the groups with mABI and the group with sABI. One-way ANOVA also revealed a significant difference in education, $F(2,78)=5.76$; $p<0.006$) in between the group of HA and the group of sABI, and between the group of HA and the group with mABI.

Clinical Measures of Prospective Memory

Materials and Procedure

The clinical manifestations of PM were assessed using the Memory for Intentions Screening Test (MIST). The MIST is a timed 30-min. test. Participants are given a word-search puzzle while performing a series of time and event-based prospective memory tasks. An example of a time- based task is, " In two minutes, tell me a time of day when I can call you tomorrow." An example of an event-based task within the MIST is, "When I hand you an envelope, self-address it." Subjects are asked to respond to an event-based

task or a time-based task with either an action response or a verbal response. There are two types of time delays between the time that the tasks are given and the requested time of response. Time delays can be either 2 min. or 15 min. After the event and time- based tasks, at the end of the test, eight multiple-choice recognition questions are asked. An example of a recognition multiple choice question is, “At any point during this test, were you supposed to (1) Ask me when the session ends (2) Ask me what time the office closes (3) Ask for your medical records. According to the MIST Professional Manual (Raskin, Buckheit and Sherrod, 2010), high scores on these tasks show that an individual has successfully encoded the intention. If the recognition task score is low, this indicates that the individual did not encode the intention. After the recognition tasks, there is a final 24-hour time delay task. According to the MIST Professional Manual (Raskin et al., 2010), this element is designed to simulate prospective memory time delays in daily life.

Statistical Analysis of Clinical Measures

The statistical tests used to analyze the MIST variables across the three populations were paired-sample t-tests and one-factor ANOVAs with level of significance at $p<0.05$.

	TASK TIME	PROSPECTIVE MEMORY TASKS	SCORE/RESPONSE			E.C.
A	Time at start A:____	**"In 15 minutes, tell me that it is time to take a break."**				
B	(A+:01):	**"When I hand you a red pen, sign your name on your paper."** [*Point to examinee's word search puzzle*]				
C	(A+:02):	**"In 2 minutes, ask me what time this session ends today."**				
D	(A+:03):	**"When I hand you a postcard, self-address it."**				
CC	(C+:02):	Examinee should ask examiner what time the session ends.	**TRIAL 1**			
			Correct ☐	**2**		
			Incorrect ☐____Time:	**0**	**1**	
E	(A+:06):	**"When I hand you a Request for Records Form, write your doctors' names on it."**				
EE	(E+:02) :	[*Hand examinee Request for Records Form]* Examinee should write their doctors' names on it.	**TRIAL 2**			
			Correct ☐	**2**		
			Incorrect ☐____Time:	**0**		
F	(A+:09):	**"In 15 minutes, use that paper** [*point to word search puzzle*] **to write the number of medications you are currently taking."**				

Figure 9. Sample of MIST instructional page. MIST includes event and time based tasks, delays of different lengths and both action and verbal responses (reproduced from Raskin, 1998)

BIKE	CANOE	RUNNING	TROLLEY	YACHT
BOAT	CAMPER	SKATES	ESCALATOR	SHIP
SCHOOLBUS	CRAWLING	SPACESHIP	WAGON	MOTORCYCLE
BULLDOZER	FLYING	SUBWAY	WALKING	HELICOPTER
CAR	HORSE	TAXI	WHEELCHAIR	TRUCK
CARRIAGE	PLANE	SUBMARINE	UNICYCLE	AMBULANCE
CLIMBING	MINIVAN	TRAIN	TRACTOR	BLIMP
LIMOUSINE	SKIPPING	ROWING	FERRY	SCOOTER

Figure 10. MIST ongoing task. A sample word search puzzle used as the ongoing activity (distractor task). (reproduced from Raskin, 1998)

Electrophysiological Correlates of Prospective Memory

Materials and Procedure

Materials

Electrophysiological Recording

The physiological correlate of PM in this study was investigated using an electroencephalogram (EEG) machine. A Compumedics Neuroscan Quick-cap with 64 sewn-in cap electrodes and six external electrodes was used for electrophysiological data collection. The stimulus design was modeled after West and Ross-Munroe (2002) and displayed on a computer monitor using E-Prime software. Participants responded to the visual stimulus by pressing one of four marked options on a keyboard. Right and left eye electrodes recorded vertical and horizontal eye movement. These electrodes were placed above, below and to the side of the left eye and to the side of the right eye. Electrodes were referenced to the reference electrode in the center of the cap during the recording. When data were being analyzed, the electrodes were then re-referenced to the mastoid electrodes.

Procedure

The complete electrophysiological recording step of the experiment takes ≈ 90 min. The preparation takes a maximum of 30 min., while the test itself takes ≈ 45 min and cleanup takes 15 min.

The testing session begins with the preparation. Thirty milliliters (30ml) of Compumedics Neuromedical Supply Supplies *Quik Gel* conductive gel is placed in a ceramic microwave safe container and warmed for 20 seconds. Two blunt needles (BD 16G ¾ Blunt Square Grind *Precision Glide* Needle), attached to syringes (BD 10ml Syringe *Luer-Lok* Tip, Latex free) are filled with 10ml of conductive gel. The participant is asked to wipe their face using a face wipe, especially at the sites of electrode placement: the temples and above and below the eyes, and forehead where the front of the cap will rest. To achieve better impedences, subjects are asked to abrade their head using a wide tooth hairbrush. The subject's head is then measured from the nasion (nose) to the back of the participant's head to establish the correct position of the cap. The circumference of the subject's head is then measured. Next, 10% of the circumference is then calculated and that distance is measured from the back of the head to the front of the head. The cap is then placed to fit these measurements. This leads to the cap fitting snugly with the front of the cap on the subject's forehead above the bridge of the nose.

After the cap is fitted, the six external electrodes are placed around the eyes and on the mastoid bones behind the ears. The electrodes that are placed around the eyes are placed on the side of the left eye (HEOL), on the side of the right eye (HEOR), placed below the left eye (VEOL), and placed above the left eye, (VEOU). The mastoid

electrodes (M1 and M2) are placed on the left and right mastoid bone, respectively. Each external electrode is secured in place using Compumedics v-shaped electrode washers. These hold the electrodes in place and allow for conductive gel to be inserted into each external electrode.

After the cap has been placed, it is plugged into the Neuroscan head box. The SynAmpRT amplifier connects to the headbox. Both pieces of hardware are connected to Scan 4.5 software, which monitors the electrode impedence. When the cap is connected, without gel, the impedence for each electrode is approximately 50.0 (kOhms). This is displayed as a magenta color within the Scan 4.5 software impedence montage. A small amount of gel is inserted so that no gel escapes from underneath any electrode. Excess gel compromises through salt bridging if the gel becomes interconnected across the electrodes and cap. Since salt bridging compromises readings, the amount of gel inserted is carefully monitored.

With gel, the impedance reading should drop below 50 kOhms. This drop in impedence changes the color of the electrode montage .The darkest shades are navy blue and black, which accompany impedence readings as low as 5kOhms.

Electrophysiological Measure Experimental Design

The experimental stimuli were modeled after West and Ross-Munroe (2002). Each subject was given 10 trails. Within each trial are 102 word pairs that contain the intention formation, ongoing activity, and PM cues.

The ongoing activity and PM trials are comprised of pairs of words that are either semantically related or unrelated. These word pairs appear on a computer screen after the spacebar key is pressed. The word pairs appear in the center of the screen, horizontally, one on top of the other. The selection of word pairs was created through the collaboration of Navneet Kaur ‘12 and Dr. Robert West. Several words were changed after a trial due to the potential to trigger unpleasant emotional responses based on their semantic meaning. As a result, any words perceived to be explicitly linked to trauma and violence were omitted.

The ongoing activity trials were shown in several colors: green, glue, red, and purple. At the beginning of each session the participant is directed with standard instructions. These instructions tell the participant to press the key labeled ‘same’ (the ‘n’ key covered with a label ‘same’) with their right index finger if the word pair is related in its semantic meaning. They are also instructed to press the key labeled ‘different’ (‘m’ key covered with a label ‘different’) with their right middle finger, if the word pair is not related semantically. For example, when the word pair of *opal* in blue and *topaz* in purple appears, the participant should press the *same* key since they are both in the same category, or are semantically related. Conversely, when the word pair of *physics* in red, and *rose* in green is presented, the participant should press the different key since they are semantically unrelated.

The intention formation trials used different experimental stimulus. Here, instead of seeing a word pair, the participant is presented with one of two letter-strings (c-c-c-c-c-c-c or v-v-v-v-v-v-v). These letter strings are displayed in light grey or magenta. The participant is then instructed to press the key associated with the color the next time a

word pair in the color is seen. For example, if c-c-c-c-c-c is presented in magenta, and a word pair in magenta appears a few pairs afterward, the subject should press the letter ‘c’. After the letter string is seen, as part of the intention formation, the participant must press either ‘c’ or ‘v’ depending on which letter-string was on the screen. This step was part of the experimental design of Kaur (2012) and differs from that of West and Ross Munroe

(2002). In their experimental design, the ‘n’ or ‘m’ key needed to be pressed to move past the intention formation stage.

The PM cue trial consisted of the word pairs displayed in either grey or magenta. The color of the presented word pair depended on the color of the preceding intention formation word string, which was either grey or magenta. Participants were asked to forego a semantic judgment for these word pairs and click the letter c or v depending on the letter in the preceding intention formation trial. This could either have been a string of grey or magenta v-v-v-v-v-v or a string of grey or magenta c-c-c-c-c-c. After each response, the word pair or letter string for the next trial then appears. As training for the entire test, a practice run that contains each trial type precedes the test.

This stimulus design based on the protocol of West and Ross-Munroe (2002) measures prospective memory using event based tasks. The present design similarly contains a short time delay between the appearance of a PM cue and the chance to realize the intention. The MIST provides an opportunity to examine PM performance with longer time delays. The 24 hr. time delay complements the short time delays (10-20 seconds) of the physiological measure. Thus, the combination of behavioral and physiological PM measurement is able to provide a fairly rounded assessment of PM.

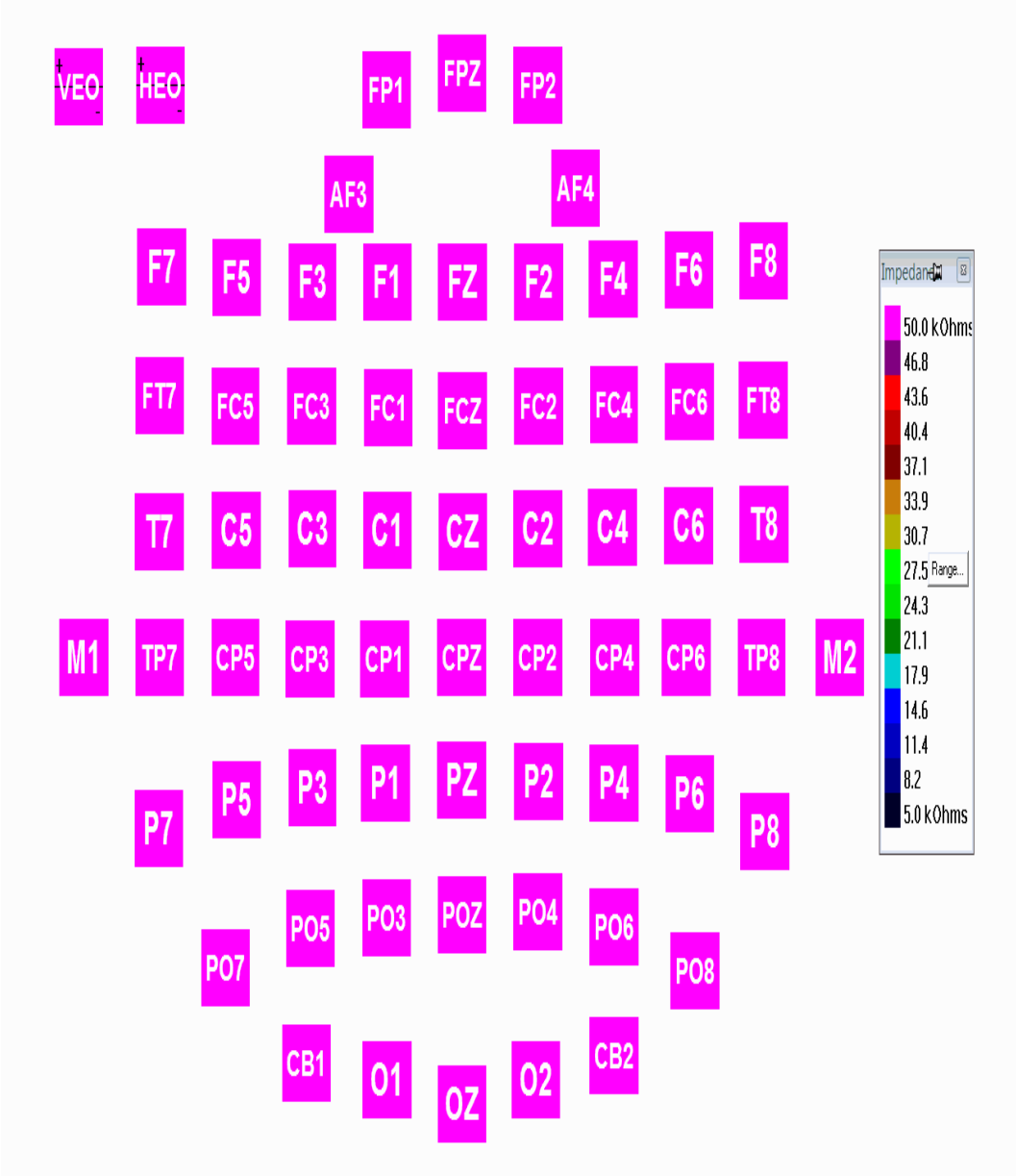

Figure 10. Neuroscan Scan 4.5 EEG cap 1-20 montage showing impedence reading at 64 electrodes before gel is inserted

Electrophysiological Data Analysis

The data analysis in this experiment was modeled after those used West & Ross-Munroe, (2002). Firstly, ERP analysis epochs were extracted from each subject's recorded session. These epochs included 200 msec of prestimulus activity and 1,200 msec of poststimulus activity. The files were processed by baseline correction. Following the analysis protocol of Kaur (2012), any files contaminated by excessive eye movement artifacts and files with peak amplitudes in excess of ±75 microvolts within the range of 200 and 1200 msec were rejected. After EEG files were processed, average files were made. An average file was made for each stimulus type, related, non-related and PM cue. For each average file, approximately 1000 epochs (samples) were averaged. In this study, each epoch is considered a trial, therefore in this context; each trial is considered a sample. Next, each of these average files were then low-pass filtered at 20Hz. Next, for each average file, calculations for the mean amplitude of N300, LPC and slow-wave were made and these values entered into SPSS.

In accordance with West and Ross-Munroe (2002), statistical tests were carried out on mean voltages averaged over 50 msec time windows. The specific ERPs (N300, Late Positive Component (LPC), Slow Wave (SW) were then examined relative to the mean voltage of the 200 msec prestimulus baseline activity (N300=275-325 msec, Late Positive Component=550-600 msec, slow wave=575-625 msec). This examination then generated amplitudes that provided a quantitative value for the modulations of the specific ERPs and electrodes in question for this study.

The electrophysiological measure of this study measured correct and incorrect PM responses (PM hits or misses) and the ongoing activity. PM hits or misses are referred to as realized and unrealized intentions, and the ongoing activity consisted of words that are relater or unrelated (same or different). The ongoing activity measurement allowed for analysis of engagement in the ongoing task, and disengagement from the ongoing task and PM cue detection. Measuring ERPs and behavioral data during the ongoing activity also facilitated comparisons between two elements of PM, the continuous activity and delay element, and the PM recognition and performance element. Using the aforementioned ERPs, these behavioral elements were compared at specific electrodes. The ERPs, behavioral variables and electrodes examined in this study were: PM hit ERP N300, electrodes P07, P08, O1, O2, P03 ,P04,: PM miss and ongoing activity ERP N300, electrodes P07, P08, O1, O2, P7, P8, P03,P04, PM hit, PM miss and ongoing activity ERP LPC, electrodes P3,P4,CP1,CP2, M1,M2, FT7, FT8; and PM miss and ongoing activity ERP slow wave, electrodes FP1, FP2, AF3 and AF4.

After the aforementioned analysis, the resulting amplitudes for these ERPs and electrodes were then input into SPSS and analyzed to calculate significant differences between HA, mABI and sABI and to identify correlations between electrophysiological and MIST data.

Normality tests revealed that the variables were not normally distributed. As a result, statistical tests for electrophysiological data were performed using Friedman's Two-Way Analysis of Variance by Ranks tests with a significance level of $p<0.05$ to compare ERP amplitudes across trials. The Independent Samples Median Test was used to compare ERP amplitudes across the three groups and electrode locations. In addition,

the Related-Samples Hodges-Lehman Median Difference Test was performed to compare amplitudes across brain regions and calculate their statistical significance. To investigate group differences, descriptives were calculated, using SPSS version 22. To examine group relationships and significance, Kruskal Wallis Tests were carried out. The Holm-Bonferroni method of sequentially adjusting p-values, followed by paired comparisons was used to test for significant differences among the groups for specific response variables and ERPs. The level of significance for these paired comparisons was $p<0.0167$, using the Bonferroni adjustment.

Results

Clinical Measure

MIST

Data for all three groups on the MIST is presented in Figures 10 and 11. One-way ANOVA revealed significance on all subscales of the MIST. The group with severe ABI performed significantly more poorly than either the HA group or the mABI group. The latter two groups were not significantly different from each other. One way ANOVA revealed significance for MIST 2 minute task $F(2,78)=5.9$; $p<0.05$), MIST 15 minute task $F(2,78)=12.3$; $p<0.05$, MIST time $F(2,79)= 9.4$; $p<0.05$, MIST event $F(2,78)=7.7$; $p<0.05$), MIST Verbal $F(2,78)= 4.7$; $p<0.05$), MIST action $F(2,78)=13.8$: $p<0.05$) (Figure 10).

*p<.05, **p<.01, ***p<.001. *. One-way ANOVA post hoc test significance at the 0.05 level. **. One-way ANOVA post hoc test significance at the 0.01 level.

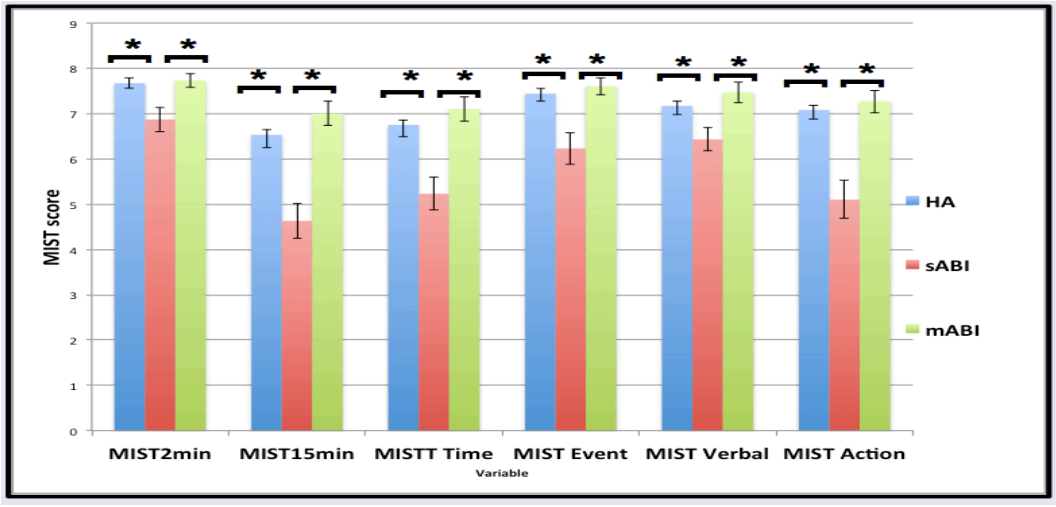

Figure 10. Mean scores in performance on MIST variables in HA, individuals with sABI, and individuals with mABI

On additional subscales of the MIST, one way ANOVA revealed significance differences in performance $F(2,78)=1.8$; $p<0.05$ between the group with sABI and HA(Figure 11). Those with sABI performed more poorly than either the HA group or the mABI group.

The latter two groups were not significantly different from each other. On the 24 hour MIST recognition task, there was no significant difference between the three groups.

*p<.05, **p<.01, ***p<.001. *. On-way ANOVA post hoc test significance at the 0.05 level. **. One-way ANOVA post hoc test significance at the 0.01 level

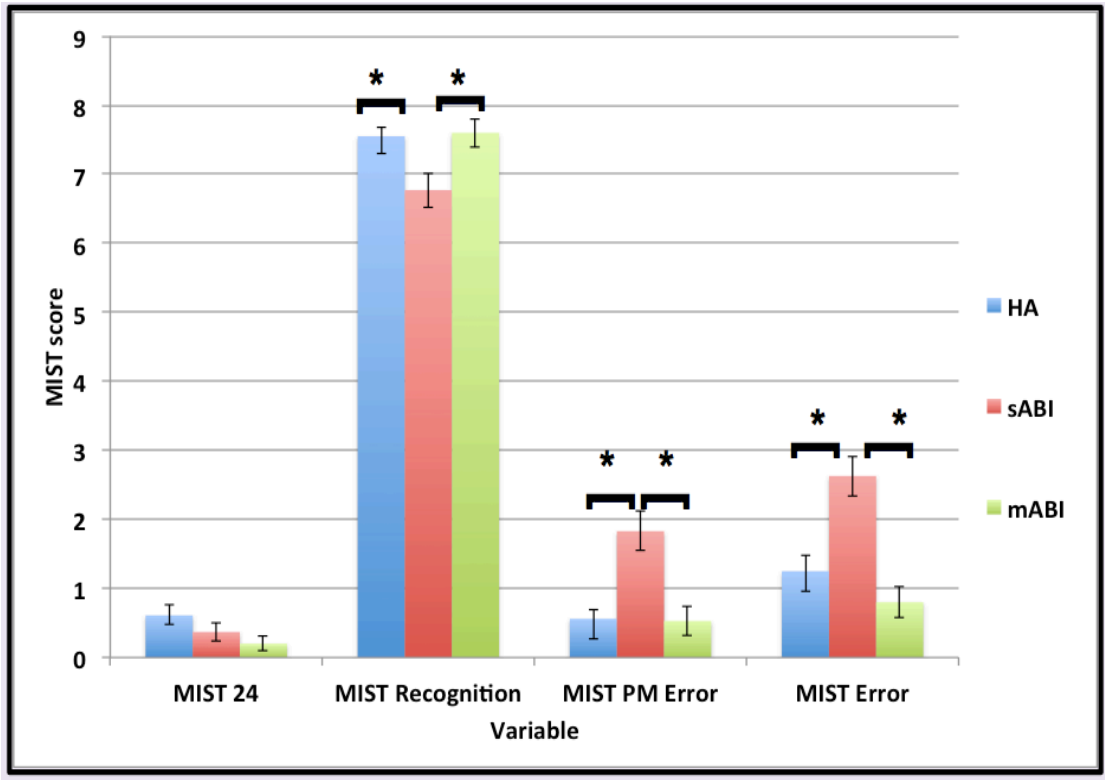

Figure 11. Mean Scores in Performance on Additional MIST Variables in HA, Individuals with sABI and Individuals with sABI and individuals with mABI

Behavioral Measure

Computerized Behavioral Measure

Data for computerized behavioral measure are presented in Figures 12 and 13. One way ANOVA revealed significance on all behavioral subscales: accuracy for ongoing task for related words $F(2,78)=19.1$: $p<0.05$, accuracy for ongoing tasks unrelated words $F(2,78)=5.1$; $p<0.05$, accuracy on PM task $F(2,78)=4.1$; $p<0.05$ (Figure 12). The group with sABI showed lower accuracy, indicating that they performed significantly poorer than either the HA group or the group with mild ABI. The latter two groups were not significantly different from each other.

*p<.05, **p<.01, ***p<.001. *. One-way ANOVA post hoc test significance at the 0.05 level. **. One-way ANOVA post hoc test significance at the 0.01 level.

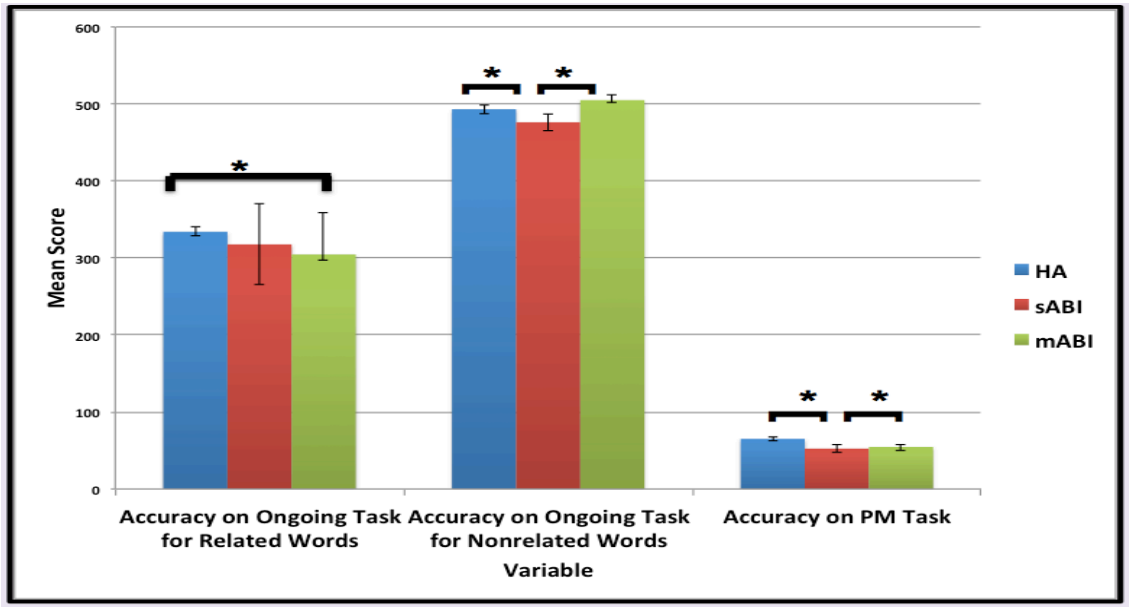

Figure 12. Mean Scores on the Computerized Behavioral Data in HA, Individuals with sABI and Individuals with sABI and individuals with mABI

One way ANOVA revealed significant differences on additional computerized behavioral subscales: Reaction time (RT) for the ongoing related hit $F(2,78)=19.1$; $p<0.05$, RT for ongoing related miss $F(2,78)= 12.3$; $p<0.05$, RT for ongoing nonrelated hit $F(2,78)= 16.6$; $p<0.05$), RT ongoing nonrelated Miss $F(2,78)=17.3$; $p<0.05$), RT PM Hit $F(2,78)=6.1$; $p<0.05$), RT PM Miss $F(2,78)=18.8$; $p<0.05$)(Figure 13). One way ANOVA revealed significant differences between the group with severe ABI showed lower accuracy, indicating that they performed significantly poorer that either the Healthy Adult group or the group with mild ABI. The latter two groups were not significantly different from each other.

*p<.05, **p<.01, ***p<.001. *. One-way ANOVA post hoc test significance at the 0.05 level. **. One-way ANOVA post hoc test significance at the 0.01 level.

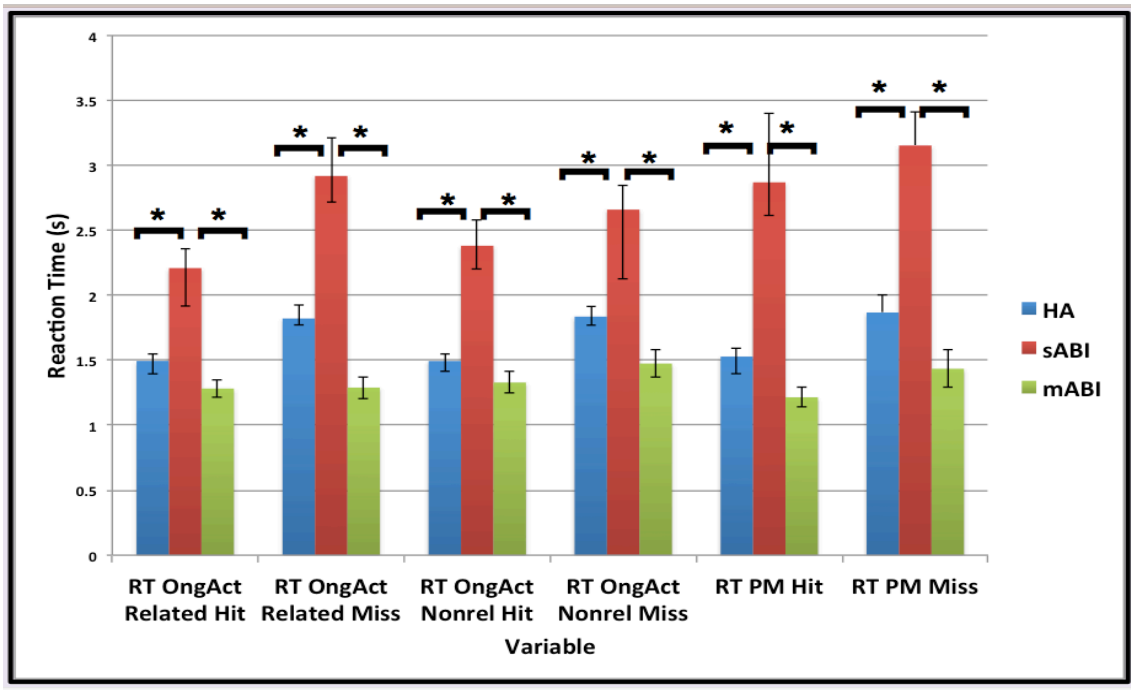

Figure 13. Mean Score in the Reaction Time for Hit and Miss Responses Obtained from the Computerized Data in HA, Individuals with sABI and Individuals with sABI and individuals with mABI

Electrophysiological Measure

One way ANOVA revealed significance for all three groups for the N300 ERP for significant electrodes and trials is presented in Figure 14: Unrelated N300O2 $F(2,78)= 2.6$; $p<0.05$, Unrelated N300PO4 $F(2,78)= 2.7$; $p<0.05$, Ongoing unrelated O2 $F(2,78)=2.6$; $p<0.05$, ongoing N300PO3 $F(2,78)=6.5$; $p<0.05$, ongoing N300PO4 $F(2,78)= 4.8$; $p<0.05$. Significant trials included unrelated trials at occipital and parietal leads: O2, PO4, O2 PO3, PO4.

On electrophysiological measures, the group with severe ABI showed lower ERP amplitudes on the N300 than either the Healthy Adult group or the group with mild ABI. The N300 amplitude of the latter two groups was not significantly different from each other.

*p<.05, **p<.01, ***p<.001. *. One way ANOVA post hoc test significance at the 0.05 level . **. One way ANOVA post hoc test significance at the 0.01 level.

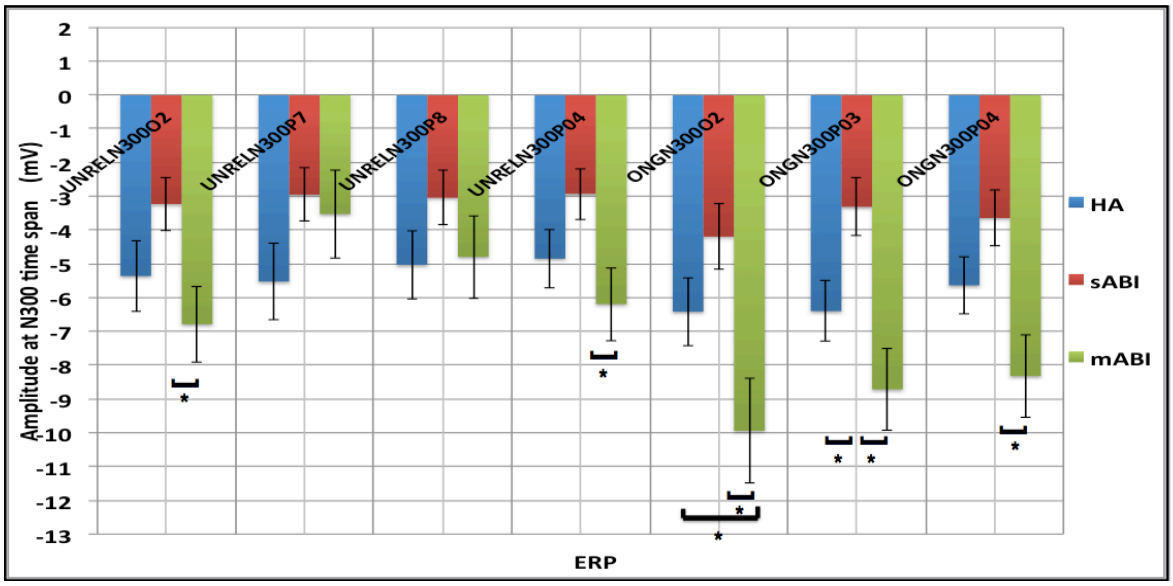

Figure 14. Amplitude (mV) at the N300 Time Span (275-325 ms after stimulus onset) for ERPs at electrodes O2, P7, P8, PO4, 02, PO3, PO4

Results of the Friedman's Two-Way Analysis of Variance by Ranks tests (Figure 15) revealed that amplitude was not greater in realized or unrealized intention trials than in ongoing trials, but there were significant differences across the trials. The N300 amplitude was not greater for realized or unrealized intention trials than for ongoing trials. Significant differences were found among the three conditions for electrodes O1 and P7. For these electrodes, realized trials resulted in greater negative amplitude than unrealized trials, and ongoing trials had greater negative amplitude than unrealized trials for the N300 waveform. Additionally, for electrodes P08 and P03, realized trials had greater negative amplitude than unrealized, but no other significant differences found for the N300 waveform.

For each condition using the Friedman's Two-Way Analysis of Variance by Ranks tests (realized, unrealized, ongoing activity) at electrodes (O1, O2, P07, P08, P03, P04), results revealed no significant differences. Additionally, the N300 amplitude during intention (PM) trials was not reduced for individuals with sABI compared to HA.

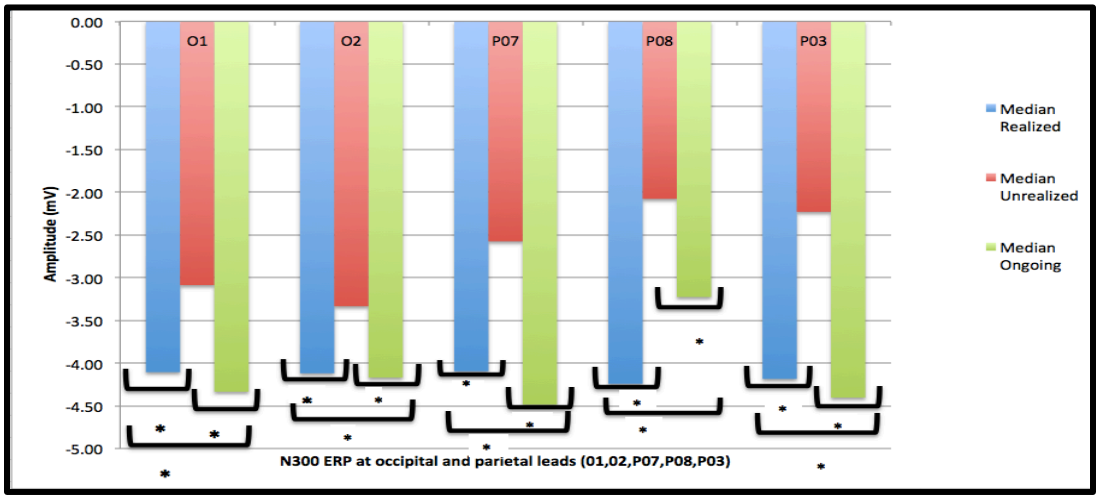

Figure 15. Showing median amplitudes for realized and unrealized intention trials and ongoing trials at electrodes O1, O2, P08, P03

Late Parietal Component (LPC)

Using Freidman's Two Way Analysis of variance by Ranks test, LPC amplitude was not greater for realized or unrealized intention trials than for ongoing trials but significant differences were found among the three conditions. For the LPC waveform, at electrodes CP1and FT7, realized trials resulted in greater negative amplitude than unrealized trials and ongoing trials, but no differences existed between ongoing and unrealized trials.

At electrode P3, in the parietal lobe, realized trials had greater negative amplitude than unrealized, but no other significant differences were found. Additionally, at P3, for the realized intention trial, there was significant difference between individuals with sABI and HA ($p<0.05$). Results revealed that at P3 the LPC median amplitude for HA was more negative than for individuals with sABI, with the difference between the two medians falling between -3.201 and -0.217μV.

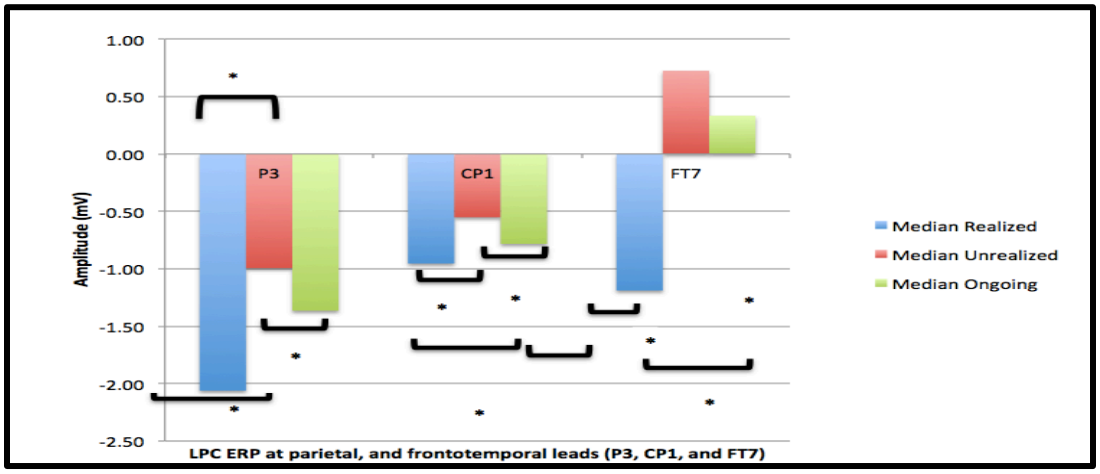

Figure 16. Showing median amplitudes for realized and unrealized intention trials and ongoing trials for the LPC ERP at electrodes P3, CP1, FT

Slow Wave (SW)

Friedman's Two-Way Analysis of Variance by Ranks, performed for each set of variables using the same electrode revealed greater negativity on realized intention trials than unrealized intention trials (with greater amplitude for realized intentions trials was not found). The amplitude of the SW during intention trials in individuals with sABI was not reduced in individuals with sABI compared to HA. Friedman's Two-Way Analysis of Variance by Ranks revealed significant differences ($p<0.05$) among the three conditions at electrodes FP1, FP2, AF3, AF4*)* and that for the SW waveform, ongoing trials had more negative amplitudes than the realized trials.

Related Slow Wave (SW) at AF4

Friedman's Two-Way Analysis of Variance by Ranks, performed for each set of variables using the same electrode, revealed that HA and individuals with mABI showed no significant difference ($p>0.05$) in RT for nonrelated hits compared to individuals with mABI. Individuals with mABI produced significantly larger amplitude for the SW ERP at AF4 than individuals with sABI. Individuals with mABI produced significantly larger amplitude ($p<0.05$) for the SW ERP at AF4 than HA.

Accuracy for Non-Related Words

Descriptives were calculated, and normality tests indicated that the variables were not normally distributed. Kruskal Wallis Tests, using the Holm-Bonferroni method of sequentially adjusting p-values, were used to test for significant differences among the groups for accuracy non-related words response variables. Using this test and the Bonferroni adjustment with significance $p<0.0167$, HA showed significantly more accurate responses on nonrelated words than individuals with mABI and those with sABI. Individuals with mABI had significantly more accurate responses on nonrelated words than individuals with sABI. There was no significant differences between the accuracy on nonrelated words between HA and individuals with mABI.

LPC Amplitude for Related Words at Electrode FT8

Kruskal Wallis Tests, using the Holm-Bonferroni method of sequentially adjusting p-values and a significance of $p<0.0167$ showed no significant differences between the amplitudes of HA and individuals with sABI for the Related LPC at electrode FT8. Individuals with mABI showed larger amplitudes (more positive) than individuals with sABI for the Related LPC ERP at electrode FT8. Individuals with mABI had significantly larger amplitudes (more positive) than HA for the Related LPC ERP at electrode FT8.

SW Amplitude for Related Words at Electrode Fronto-Parietal Lead (FP1)

Kruskal Wallis Tests, using the Holm-Bonferroni method of sequentially adjusting p-values and a significance of $p<0.0167$ showed that the amplitudes for the SW ERP for related words at electrode FP1 were not significantly different between HA and individuals with sABI. Individuals with mABI had significantly larger amplitudes for the SW for related words at electrode FP1compared to individuals with sABI. Individuals with mABI were found to have significantly larger amplitudes for SW ERP for related words at electrode FP1compared to HA.

SW Amplitude for Related Words at Anterior Frontal Lead (AF3)

Kruskal Wallis Tests, using the Holm-Bonferroni method of sequentially adjusting p-values and a significance of $p<0.0167$ showed revealed no significant differences in amplitude were for the SW ERP for related words at electrode AF3 for individuals with sABI and HA. Individuals with mABI had significantly larger amplitudes (more positive) than individuals with sABI for the SW ERP at electrode AF3. Individuals with mABI had significantly larger amplitudes (more positive) than HA for the SW ERP at electrode AF3.

Discussion

Significant differences on the MIST among subject groups

Individuals with sABI displayed impaired PM compared to individuals with mABI and HA on all most MIST variables. HA and individuals with mABI did not differ in most MIST variables This lack of significant difference between HA and mABI in behavioral aspects of PM supports the findings of Carroll et al. (2004), which reports few cognitive deficits extending past a few weeks post-injury, for individuals with mABI. Given that most individuals with mABI recover completely, it might be interesting to repeat this study with only those who continue to experience post-concussion syndrome.

This study's finding of significant differences in behavioral PM performance between HA and sABI support the findings of Pavawalla, Schmitter-Edgecombe & Smith (2012) and Vakil (2005). Both these studies found deficits in PM performance in individuals with sABI compared to HA.

Significant differences on the Computerized Behavioral among subject groups

Individuals with sABI differed significantly from HA on the accuracy of the prospective memory task (PM task) within the computerized test. In addition, individuals with sABI and individuals with mABI differed significantly in terms of their accuracy on the PM task, with those with mABI performing better than those with sABI. The trend of

no significant differences between HA and mABI continued into the computerized test's results. These results also agree with findings by Carroll et al. (2004) that the prognosis of mABI was good, with a small percentage of individuals with mABI experiencing cognitive impairment past three weeks post injury. Our computer PM test findings further agree with those of Pavawalla, et al. (2012) and Vakil (2005), who found that sABI had pronounced deficits compared to HA. Mean scores of reaction time (Figure 4) also mirror these results with individuals with sABI taking significantly longer than HA and individuals with sABI to respond to the ongoing task and PM cue. This offers further support to findings of Carroll et al. (2004), Pavawalla et al. (2012) and Vakil et al. (2005).

Variation in N300 Amplitude on Computerized Tests

N300 was lower in mABI and sABI at the O2 and PO4 electrode for unrelated words. Other significant differences were seen at O2, PO3 and PO4 but again, were due to the ongoing task, which carries no PM assessment value. N300 amplitude was consistently reduced for participants with sABI compared to individuals with mABI and HA at electrodes O2, P7, P8, PO4, O2, PO3, PO4. This finding of attenuated amplitude of the N300 in individuals with sABI that was not present in individuals with mABI and HA agrees with studies by West and Covell (2001), West, Herndon et al. (2003), and Zollig et al. (2012). These results also indicate a global effect of reduced amplitudes in individuals with sABI.

N300 Amplitude, Computer Test Condition and Electrode Significant differences

Electrodes O1, P7, P8 and P03 showed significant differences with realized trials (PM hits; when the participant made a correct PM response and realized the intention to click c or v when either grey or magenta words appeared). This resulted in greater negative amplitude than unrealized trials (PM misses) at these electrodes. This agrees with Zollig et al. (2012) who found reduced amplitudes in N300 in older adults with PM impairment. The location of these N300 significant amplitude differences also agrees with West (2011), who reported occipital and parietal lobe activity associated with the N300 waveform, PM activity and alerting the neural system to the presence of a cue. This supports the theory that N300 is an accurate marker for cue detection in PM. Interestingly, ongoing trials had greater negative amplitude than unrealized trials for the N300 waveform. Since during ongoing trials participants might be looking out for PM cues thus eliciting increased amplitude of N300. In contrast to the unrealized or PM misses, individuals are not alerting the neural system to a possible cue.

LPC Amplitude, Computer Test Condition and Electrode Significant differences

For the LPC at electrode P3, for the realized intention trial, there were significant differences between individuals with sABI and HA. This again supports the findings of West (2011), and Zollig et al. (2012). A novel finding was that at P3 the amplitude for HA was more negative than for individuals with sABI. In West (2011) LPC is

characterized as a positive waveform over the parietal region of the brain. In our study the more negative amplitude of LPC in HA contradicts with previous findings. To further understand the role of a significantly more negative LPC more research needs to be conducted on HA with high scores of PM.

Slow Wave Amplitude, Computer Test Condition and Electrode Significant differences

Significant differences were found among the three conditions: realized intention trials, unrealized intention trials, and ongoing activity trials at electrodes FP1, FP2, AF3, AF4 during realization trials (PM hits) compared to unrealized trials (PM misses). This agrees with West (2011) who postulated that the FSW is associated with disengagement from ongoing activity and alerting to a possible cue. Additionally, the frontal electrodes (FP1, FP2, AF3, AF4) revealed by the findings agree with the established association between frontal regions and PM (West 2011). For the SW waveform, ongoing trials had more negative amplitudes than the realized trials. This attenuation of FSW amplitude during ongoing trials can be interpreted as reflecting a participant's focus on the ongoing task, since FSW amplitude has been linked to disengagement during the ongoing activity and alerting to a possible cue. During the ongoing activity, there is little to no disengagement, thus attenuated FSW amplitude is a logical result.

Significant Differences for Computerized Behavioral Test Response Variables and ERPs, among the three subject groups

Related Frontal Slow Wave (SW) at electrode AF4

Individuals with mABI produced significantly larger amplitude for the FSW ERP at AF4 than individuals with sABI. This can be interpreted as showing that individuals with mABI had an increased ability to disengage from the ongoing activity and be alerted to a possible cue, compared to individuals with sABI. A novel finding was that individuals with mABI produced significantly larger amplitude for the SW ERP at AF4 than HA. On possible psychosocial explanation for this was that many individuals with mABI came into the testing session wanting to prove that their memories were better or 'just as good as' HA. This increase in amplitude in FSW, an ERP that indicates PM function, needs to be investigated further with individuals with mABI and HA in order to extrapolate reasons for this increase in SW amplitude in those with mABI. In order to lower the possibility of increased 'psychosocial interference' in PM performance, examiners can avoid words such as test, assessment, score and performance to hopefully not influence the participants to feel as though they need to perform at a certain level. Adjusting the semantics of the training and interaction with the examiner can hopefully lower psychosocial influence on the subjects' performance. In light of the present SW results obtained, it would also be interesting to compare groups of people with mABI who are symptomatic to those who are not symptomatic.

LPC Amplitude for related words at electrode FT8

We found that individuals with mABI showed larger amplitudes (more positive) than individuals with sABI for the Related LPC ERP at electrode FT8. This is consistent with PM performance literature (West, (2011), Cona et al., (2012)). In addition, results revealed an unexpected finding that individuals with mABI had significantly larger amplitudes (more positive) than HA for the Related LPC ERP at electrode FT8. One theory is that individuals with mABI had to recruit more frontal and temporal neural resources to execute the task of differentiating related words during the ongoing semantic activity. This might explain the higher amplitude seen in those with mABI compared to HA. Again, an exact hypothesis needs to be drawn after more examination between these two groups is conducted.

SW Amplitude for related words at electrode FP1

Individuals with mABI had significantly larger amplitudes for the SW for related words at electrode FP1 compared to individuals with sABI. The novel finding is again repeated for the SW but at another electrode, in the frontal parietal region, FP1. Individuals with mABI had significantly larger amplitudes for SW ERP for related words at electrode FP1 compared to HA. Here the aforementioned theory for increased LPC at FT8 may explain the larger SW amplitudes for related words at FP1. The frontal region of the brain is one of the most common areas to be affected in individuals with mABI

(Duff, 2004), therefore an increased amplitude may reflect the higher levels of recruitment that may be needed to identify a related word pair, compared to a HA who may recruit less neural systems on this area to complete the same task. Again, further research into differences in M between mABI and HA specifically will hopefully shed light on this finding of increased amplitude for the SW in mABI relative to sABI.

SW Amplitude for Related Words at AF3

Results indicated that individuals with mABI had significantly larger amplitudes (more positive) than individuals with sABI for the SW ERP at electrode AF3. This is logical as the SW is associated with the ability to disengage from the ongoing activity. The ability to disengage from the ongoing activity was expected to be less impaired in individuals with mABI compared to those with sABI. Therefore it is expected that individuals with mABI show higher amplitudes and therefore increased ability to disengage from the ongoing activity, relative to those with sABI. While this seems logical and provides a fairly satisfactory theory, more needs to be gleaned about the relationship between these two populations: individuals with mABI and individuals with sABI, and their interaction with PM and SW amplitude.

Age Influence on MIST, Behavioral and Electrophysiological correlates of PM

The significant differences in age between HA and mABI and between mABI and sABI ($p<0.001$) may have had a possible influence on the overall lack of significance between HA and mABI on both clinical and electrophysiological PM variables. Cona et al. (2012) showed that younger individuals showed prefrontal sustained PM ERPs that were absent in older adults. Cona et al. (2012) also found that as a result older adults were impaired on strategic monitoring systems during the ongoing task. This impairment can be then be seen to influence and lead to reduced PM performance. This impairment in PM function may offer an explanation to the lack of difference in PM variables between HA and mABI, since the mABI group was significantly younger that the sABI group. As a consequence of their age, their PM function, despite having a mABI, might have been less impaired than the older sABI individuals to begin with. Therefore it is logical that the younger individuals with mABI were not found to be different from HA since their initial PM functioning may have been less impaired than sABI and therefore similar to HA performance, due to the aforementioned age-related PM differences.

Conclusion

The results of our study successfully supported the hypotheses, overall allowing a greater insight into the PM of three populations. The results of this experiment showed that individuals with sABI have PM impairment compared to HA and individuals with mABI. Results also revealed that those with mABI are not significantly different from HA in terms of PM which is a very hopeful finding in light of the high rates of mABI, in particular sport related concussions in young, developing school-aged persons. In terms of significant ERPs and PM performance, our results were mainly in keeping with the literature of PM and ERP analysis, finding relationships between the frontal, parietal and occipital lobes and PM performance across the groups. The behavioral finding of difference between sABI and HA and sABI and mABI, but not mABI and HA was also found in ERP data. Reduced amplitudes at the brain regions associated with PM was reported consistently.

A novel finding of this study was increased amplitude in mABI compared to HA for the LPC and SW over frontal and frontotemporal regions of the brain during related word trials within the ongoing task. Further analysis is needed to examine the differences between these groups that have both similarities and differences. Additionally, the effect of age on PM may have been a contributing factor to the lack of significant difference between HA and mABI since the mABI population was significantly younger than the HA and sABI populations. According to the literature younger individuals have reduced impairment on PM tasks therefore the difference in age may have influenced the results.

Further research using groups of individuals with ABI who are not significantly different in age would shed light on the effect of age on PM in populations with mABI and sABI.

Implications and Future Work

The findings of this study, which indicate explicit areas of impairment in individuals with sABI, have the potential to aid in cognitive remediation design specific to the deficits of this population. Remediation that is tailored to the particular behavioral and neural correlates affected after a sABI has the potential to be more effective in improving overall PM function. This study can be used as a tool to pinpoint areas of PM deficits in individuals with ABI who suffer greatly in terms of their independence and sense of self.

In terms of future work, improving the electrophysiological experimental design would be beneficial. One observation that was made when testing individuals with sABI was that the semantic task structure of the test might have been too challenging. Additionally, the length of the test was too taxing for this population. Sitting still and focusing on a computer screen in excess of an hour is too rigorous a cognitive activity for someone who has suffered and survived a sABI. In particular, individuals with sABI became fatigued during the last few trials. Redesigning an experimental structure that is shorter and less semantically taxing while still preserving the reliability, validity and specificity of the former design will be beneficial and more appropriate for testing PM in individuals with sABI.

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